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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,935	10/12/2001	Donald E. Staunton	27866/36470A/US	1821

4743 7590 02/16/2006

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EXAMINER	
BRUSCA, JOHN S	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,935	STAUNTON, DONALD E.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *6,8,9,18,19,22-25,30-32,36-47 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,10-17,20,21,26-29,33-35 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is non-final because it contains a new grounds of rejection under 35 U.S.C. 112, first paragraph not necessitated by the applicant's amendment.

2. For the purpose of examination, the term "allosteric" is defined in Example 1, pages 81-84 as a property of a protein that may be determined by determining sufficient similarity of a query protein to known allosteric proteins.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-5, 7, 10-17, 20, 21, 26-29, 33, and 34 in the Office action mailed 19 May 2005 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the arguments presented by the applicants in their response filed 25 November 2005. The rejection of claims 35 and 48 on the previous grounds is maintained below.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3-5, 7, 12-17, 20, 21, 26-29, 33-35, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 35 and 48 are drawn to a method of contacting FtsZ protein with an effector that interacts with an allosteric regulatory site of the protein and modulates binding of the protein

with a binding partner. In some embodiments the effector of the FtsZ protein is a small molecule, a diaryl compound, a diarylamide, or a diarylsulfide compound. In one embodiment the binding partner is GTP.

The specification describes in Table 1 on pages 30-66 lists 96 classes of proteins with alpha beta structures. The specification describes 17 working examples of methods of modulating binding of first molecules as claimed:

1) CD11B in example 3, pages 87-89 and example 16, pages 127-128

2 and 3) C2 and factor B in example 4, pages 89-96

4-11) seven integrins in example 9, pages 107-111 (see Table 5, page 111)

12-13) two integrins in example 11, pages 114-116

14) alpha 1 integrin in example 12, pages 116-122

15) Rac 1 in example 17, pages 128-131

16) HPPK in example 19, pages 133-141.

17) ENR in example 21, pages 143-145

Description of methods using 17 proteins in the specification does not include a description of a method of modulation of binding of FtsZ protein. The specification shows in example 20 on pages 142-143 a prophetic example of a FtsZ binding assay, and describes FtsZ on page 19, and further lists FtsZ in table 3 on page 84 as having sufficient similarity to allosteric proteins to classify FtsZ protein as an allosteric protein. However the specification does not describe effectors of any type of FtsZ. The specification does not describe the Rossmann fold structure of FtsZ. The specification does not describe a method utilizing FtsZ that comprises effectors, or the claimed structural limitations of FtsZ such as Rossmann folds, or the structural

limitations of an FtsZ effector such as small molecule, diaryl compounds, and diarylamide or diarylsulfide structures.

Claims 3-5, 7, 12-17, 20, 21, 26-29, 33-35, and 48 are drawn to methods of using allosteric effector molecules that are diarylamide compounds. Amides are compounds with an acyl group linked to an NH_2 group. The specification does not show a structure or describe a working example of a diarylamide effector that regulates binding as part of the claimed method.

6. Applicant's arguments filed 25 November 2005 have been fully considered but they are persuasive only in part. With respect to description of methods of modulation of generic proteins having alpha/beta domains by effectors other than diarylamides, the rejection has been withdrawn. However description of a method of using a genus does not equate to description of every individually claimed member of the genus, and the rejection for lack of written description of claims 35 and 38 limited to methods of modulation of binding activity of FtsZ proteins is maintained. The applicants point to Table 3 in Example 1 as providing evidence in the specification at the time of filing that FtsZ is an allosteric protein. The applicants further point to an article by Lowe et al. for evidence in the prior art that FtsZ has a Rossmann fold and has similarity to other proteins described in the instant specification. However the specificity of claims 35 and 38 to methods of modulation of FtsZ binding requires a corresponding specificity in the description to describe the claimed method for the FtsZ protein. The specification does not describe modulation of binding of FtsZ to a binding partner, and does not describe any structure of an effector that would cause such modulation. In University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004), the CAFC found that claims drawn to a method of using compounds that inhibit prostaglandin H synthase-2 were not described because the specification

did not describe the compounds. Similarly, the instant claims for a method of modulation of FtsZ binding activity is not described because the instant specification does not describe compounds that are used in the claimed method. Regarding diarylamide effectors, the specification does not describe such effectors, or methods of their use.

Claim Rejections - 35 USC § 102

7. The rejection of claims 1, 4, 10, 13, 14, 15, and 28 under 35 U.S.C. 102(b) as being anticipated by Coller as evidenced by Hynes in the Office action mailed 19 May 2005 is withdrawn in view of the amendment to the claims filed 25 November 2005.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 4, 5, 7, 10, 11, 13-17, 20, 21, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamilton et al. in light of Lee et al.

The claims are drawn to a method of using an effector that modulates the binding of a protein that comprises an alpha/beta domain and an allosteric regulatory site to a binding partner. In some embodiments the effector is a small molecule, or is a diaryl compound. In some embodiments the protein comprises a Rossmann fold structure in a 321456, 231456, or a 32145 orientation. In some embodiments the effector decreases binding between the protein and the binding partner.

Hamilton et al. shows in the abstract and throughout compounds that inhibit binding of the integrin Mac-1 to neutrophils. On page 1652 Hamilton et al. shows that the binding is

contributed by Mac-1 in two assays. Platelet activating factor (PAF) activated neutrophils were blocked from binding serum coated plastic wells by anti-Mac-1 antibodies, and tumor necrosis factor (TNF) activated neutrophils were blocked from binding serum coated plastic wells by anti CD11b antibodies (Mac-1 comprises CD11b and CD18). Hamilton et al. assayed a number of small molecules for effect on binding of PAF and TNF treated neutrophils in tables 1-4. Compounds 4-9 in table 1, 10-22 in table 2, and compounds 23, 24, and 26 in table 3 are diaryl small molecules that inhibit binding of TNF activated neutrophils. Compounds 11, 17, 19, 22, NPC 15669, and NPC 17923 in Table 4 are diaryl small molecules that inhibit binding of PAF activated neutrophils.

Lee et al. shows in the abstract and throughout the structure of two conformations of the integrin Mac-1 I domain. Lee et al. shows on page 1334 that Mac-1 comprises a Rossmann fold and an I domain. Figure 4 shows that the I domain comprises alpha helical and beta sheet regions.

Regarding the allosteric regulatory site, the specification defines allosteric proteins as proteins with a high level of similarity to proteins that are known allosteric proteins in Example 1, pages 81-83. On table 3, page 84, the specification identifies Mac-1 as an allosteric protein. The claimed method limitations that are not explicitly described Hamilton et al. are inherent properties of Mac-1 as discussed above. The MPEP states in 2112.01:

> V. ONCE A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Conclusion

10. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.Any inquiry concerning this communication or earlier communications from the examiner

should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

John S. Brusca 10 February 2006

John S. Brusca
Primary Examiner
Art Unit 1631

jsb